

WHAT IS CLAIMED IS:

1. A therapeutic composition useful for treatment of a mucositis at a mucosal site, the composition comprising:

at least one pharmaceutical substance, effective to provide therapeutic effect for at least one of the prevention of the mucositis and treatment of the mucositis; and

at least one biocompatible polymer that is different than the pharmaceutical substance.

2. The therapeutic composition of Claim 1, comprising a carrier liquid.

3. The therapeutic composition of Claim 1, wherein the mucositis comprises a disorder selected from the group consisting of oral mucositis, esophagitis, cystitis, sinusitis, asthma, colitis, GERD, proctitis, stomatitis, celiac disease, inflammatory bowel disease, and Crohn's disease.

4. The therapeutic composition of Claim 1, wherein the pharmaceutical substance is selected from the group consisting of an antibacterial, an anti-inflammatory, an antioxidant, an anesthetic, an analgesic, a protein, a peptide and a cytokine.

5. The therapeutic composition of Claim 1, wherein the pharmaceutical substance comprises a thiol-containing compound.

6. The therapeutic composition of Claim 5, wherein the thiol-containing compound is selected from the group consisting of N-acetylcysteine, and glutathione.

7. The therapeutic composition of Claim 1, wherein the pharmaceutical substance comprises a sulfur-containing antioxidant.

8. The therapeutic composition of Claim 7, wherein the sulfur-containing antioxidant is selected from the group consisting of S-carboxymethylcysteine and methylnmethionine sulfonium chloride.

9. The therapeutic composition of Claim 7, wherein the sulfur-containing antioxidant includes sulfur in at least one functional group selected from the group consisting of thiol, thioether, thioester, thiourea, thiocarbamate, disulfide, and sulfonium salt.

10. The therapeutic composition of Claim 1, wherein the pharmaceutical substance comprises a precursor for glutathione biosynthesis.

11. The therapeutic composition of Claim 10, wherein the precursor is selected from the group consisting of N-acetylcysteine, procysteine, lipoic acid, s-allyl cysteine, and methylnmethionine sulfonium chloride.

12. The therapeutic composition of Claim 1, wherein the pharmaceutical substance is N-acetylcysteine.

13. The therapeutic composition of Claim 1, wherein the therapeutic effect comprises a decrease in the severity of at least one of inflammation, infection and ulceration from the mucositis at the mucosal site experienced by the host relative to no treatment for the mucositis.

14. The therapeutic composition of Claim 13, wherein the therapeutic effect comprises a decrease in the duration that the host experiences at least one of inflammation, infection and ulceration from the mucositis at the mucosal site relative to no treatment for the mucositis.

15. The therapeutic composition of Claim 1, wherein the pharmaceutical substance comprises from about 0.001 percent by weight to about 50 percent by weight of the composition.

16. The therapeutic composition of Claim 1, wherein the therapeutic composition exhibits reverse-thermal viscosity behavior over at least some range of temperatures between 1°C and 37°C.

17. The therapeutic composition of Claim 1, wherein the therapeutic composition exhibits reverse-thermal viscosity behavior over at least some range of temperature between 1°C to 20°C.

18. The therapeutic composition of Claim 1, wherein the biocompatible polymer is a reverse-thermal gelation polymer.

19. The therapeutic composition of Claim 18, wherein the biocompatible polymer, as formulated in the therapeutic composition, has a reverse-thermal liquid-gel transition temperature within a range of from 1°C to 37°C, so that the therapeutic composition gels as the temperature of the therapeutic composition is increased from below to above the reverse-thermal gel transition temperature.

20. The therapeutic composition of Claim 18, wherein the biocompatible polymer, as formulated in the composition, does not impart reverse-thermal gelation properties to the composition.

21. The therapeutic composition of Claim 18, wherein the biocompatible polymer is a polyoxyalkylene block copolymer.

22. The therapeutic composition of Claim 18, wherein the biocompatible polymer comprises from 5 weight percent to 25 weight percent of the composition.

23. The therapeutic composition of Claim 1, wherein the biocompatible polymer comprises from 1 weight percent to 70 weight percent of the composition.

24. The therapeutic composition of Claim 1, wherein the therapeutic composition comprises a carrier liquid and the biocompatible polymer is dissolved in the carrier liquid when  
5 the composition is at a temperature of 5°C.

25. The therapeutic composition of Claim 1, wherein the pharmaceutical substance is dissolved in the carrier liquid when the composition is at a temperature of 5°C.

26. The therapeutic composition of Claim 1, comprising a penetration enhancer.

27. The therapeutic composition of Claim 26, wherein the penetration enhancer is  
10 different than each of the pharmaceutical substance and the biocompatible polymer.

28. The therapeutic composition of Claim 26, wherein the penetration enhancer is selected from the group consisting of a chitosan; a chitosan derivative; a fatty acid; citric acid; a salicylate; a caprylic/capric glyceride; sodium caprylate; sodium caprate; sodium laurate; sodium glycyrrhetinate; dipotassium glycyrrhizinate; glycyrrhetinic acid hydrogen  
15 succinate, disodium salt; an acylcarnitine; a bile salt; and a phospholipid.

29. The therapeutic composition of Claim 26, wherein the penetration enhancer is a chitosan or a chitosan derivative.

30. The therapeutic composition of Claim 26, wherein the penetration enhancer comprises from about 0.01 percent by weight to about 10 percent by weight of the therapeutic  
20 composition.

31. The therapeutic composition of Claim 1, comprising a bioadhesive agent that is different than the pharmaceutical substance and the biocompatible polymer.

32. The therapeutic composition of Claim 31, wherein the bioadhesive agent is a polymer that aids in adhering the therapeutic composition to a mucosal surface at the mucosal  
25 site and holding the pharmaceutical substance adjacent the mucosal surface.

33. The therapeutic composition of Claim 31, wherein the bioadhesive agent is selected from the group consisting of poloxamers, mucin glycoproteins, trefoil peptides, cellulose derivatives and carbomers.

34. The therapeutic composition of Claim 31, wherein the bioadhesive agent is a  
30 carbophil polymer.

35. The therapeutic composition of Claim 1, comprising at least one taste masking component.

36. The therapeutic composition of Claim 35, wherein the taste masking component is selected from the group consisting of fruit flavorings, mint flavorings, chocolate flavorings, salt  
5 and sugars.

37. The therapeutic composition of Claim 35, wherein the flavor the taste-masking component imparts a lemon flavor to the composition.

38. The therapeutic composition of Claim 1, comprising at least one preservative component.

10 39. The therapeutic composition of Claim 38, wherein the preservative component is selected from the group consisting of antioxidants, antifungals and antimicrobials.

40. The therapeutic composition of Claim 38, wherein the preservative component is sodium benzoate.

15 41. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form selected from the group consisting of an oral solution, a bladder irrigation solution, a mouthwash, a gel, drops, a spray, a suppository, a slurry, a tablet, a lozenge, a patch, a film and a lollipop design.

42. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of an oral solution.

20 43. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a mouthwash.

44. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of drops.

25 45. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a spray.

46. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a suppository.

47. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a slurry.

30 48. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a tablet.

49. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a film.

50. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a lollipop.

5 51. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a gel.

52. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a lozenge.

10 53. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a patch.

54. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a bladder irrigation solution.

15 55. The therapeutic composition of Claim 1, wherein the mucosal site is selected from the group consisting of rectal, vaginal, bladder, ocular, oral, sublingual, esophageal, nasal, gastrointestinal, pulmonary and aural mucosal sites.

56. The therapeutic composition of Claim 1, wherein the mucosal site is in the rectum and the therapeutic composition is in the form of a gel that is administrable rectally as a suppository to contact the mucosal site.

20 57. The therapeutic composition of Claim 1, wherein the mucosal site is in the vagina and the therapeutic composition is in the form of a gel that is administrable vaginally as a suppository to contact the mucosal site.

58. The therapeutic composition of Claim 1, wherein the mucosal site is in the bladder and the therapeutic composition is in the form of a bladder irrigation solution administrable to the bladder by catheter to contact the mucosal site.

25 59. The therapeutic composition of Claim 1, wherein the mucosal site is an ocular site and the therapeutic composition is administrable to the eye in the form of drops to the eye to contact the mucosal site.

30 60. The therapeutic composition of Claim 1, wherein the mucosal site is in the oral cavity and the therapeutic composition is in the form of a mouthwash administrable orally to contact the mucosal site.

61. The therapeutic composition of Claim 1, wherein the therapeutic composition is in the form of a lozenge administrable orally.

62. The therapeutic composition of Claim 1, wherein the mucosal site is sublingual and the therapeutic composition is in the form of a tablet, patch or film that can be sublingually placed to contact the mucosal site.

63. The therapeutic composition of Claim 1, wherein the mucosal site is in the nasal cavity and the therapeutic composition is sprayable into the nasal cavity to contact the mucosal site.

64. The therapeutic composition of Claim 1, wherein the therapeutic composition is in a swallowable form that is swallowable to contact the mucosal site.

65. The therapeutic composition of Claim 64, wherein the mucosal site is located in the esophagus and at least a portion of the biocompatible polymer and pharmaceutical substance adhere to mucosal surfaces in the esophagus when the therapeutic composition is swallowed.

66. The therapeutic composition of Claim 64, wherein the mucosal site is located in the gastrointestinal tract and at least a portion of the biocompatible polymer and the pharmaceutical substance adhere to mucosal surfaces in the gastrointestinal tract wherein the therapeutic composition is swallowed.

67. The therapeutic composition of Claim 1, wherein the mucosal site is in the lungs and the therapeutic composition is inhalable in the form of an aerosol to contact the mucosal site.

68. The therapeutic composition of Claim 1, wherein the mucosal site is in the ear and the therapeutic composition is administrable into the ear in the form of drops.

69. The therapeutic composition of Claim 1, wherein the host is a mammal.

70. The therapeutic composition of Claim 69, wherein the mammal is a human patient.

71. A therapeutic composition useful for treatment of mucositis at a mucosal site, the composition comprising a sulfur-containing antioxidant.

72. The therapeutic composition of Claim 71, wherein the sulfur-containing antioxidant includes sulfur in at least one functional group selected from the group consisting of thiol, thioether, thioester, thiourea, thiocarbamate, disulfide and sulfonium salt.

73. The therapeutic composition of Claim 71, wherein the sulfur-containing antioxidant is a thiol.

74. The therapeutic composition of Claim 73, wherein the thiol is N-acetylcysteine.

75. The therapeutic composition of Claim 71, wherein the sulfur-containing antioxidant is procysteine.

76. The therapeutic composition of Claim 71, wherein the sulfur-containing antioxidant is lipoic acid.

77. The therapeutic composition of Claim 71, wherein the sulfur-containing antioxidant is s-allyl cysteine.

78. The therapeutic composition of Claim 71, wherein the therapeutic composition further comprises a biocompatible polymer.

79. The therapeutic composition of Claim 78, wherein the biocompatible polymer is a reverse-thermal gelation polymer.

80. The therapeutic composition of Claim 71, wherein the therapeutic composition further comprises a bioadhesive agent.

81. The therapeutic composition of Claim 80, wherein the bioadhesive agent is a carbophil polymer.

82. The therapeutic composition of Claim 71, wherein the therapeutic composition exhibits reverse-thermal viscosity behavior over at least some range of temperatures between 1°C and 37°C.

83. A method of delivering to a mucosal site within a host a pharmaceutical substance for treatment of mucositis at the mucosal site, the method comprising:

introducing a therapeutic composition into the host, the therapeutic composition comprising the pharmaceutical substance and a biocompatible polymer, the pharmaceutical substance being effective for treating mucositis at the mucosal site;

wherein, after the introducing, at least a portion of the biocompatible polymer and the pharmaceutical substance adhere to a mucosal surface at the mucosal site.

84. The method of Claim 83, wherein the introducing comprises introducing the therapeutic composition into at least one of the rectum, vagina, bladder, orbita, oral cavity, nasal cavity, esophagus, gastrointestinal tract of the host, lungs and ear of the host.

85. The method of Claim 83, wherein the pharmaceutical substance is selected from the group consisting of an antibacterial, an anti-inflammatory, an antioxidant, an anesthetic, an analgesic, a protein, a peptide and a cytokine.

86. The method of Claim 83, wherein the pharmaceutical substance comprises a thiol-containing compound.

87. The method of Claim 86, wherein the thiol-containing compound is selected from the group consisting of N-acetylcysteine, and glutathione.

88. The method of Claim 83, wherein the pharmaceutical substance comprises a sulfur-containing antioxidant.

89. The method of Claim 83, wherein the pharmaceutical substance comprises a sulfur-containing antioxidant is selected from the group consisting of S-carboxymethylcysteine and methylnmethionine sulfonium chloride.

90. The method of Claim 89, wherein the sulfur-containing antioxidant includes sulfur in at least one functional group selected from the group consisting of thiol, thioether, thioester, thiourea, thiocarbamate, disulfide, and sulfonium salt.

91. The method of Claim 83, wherein the pharmaceutical substance comprises a precursor for glutathione biosynthesis.

92. The method of Claim 91, wherein the precursor is selected from the group consisting of N-acetylcysteine, procysteine, lipoic acid, s-allyl cysteine, and methylnmethionine sulfonium chloride.



93. The method of Claim 83, wherein the pharmaceutical substance is N-acetylcysteine.

94. The method of Claim 83, wherein the therapeutic composition exhibits reverse-thermal viscosity behavior over at least some range of temperatures between 1°C and the physiological temperature of the host.

95. The method of Claim 94, wherein when the therapeutic composition is introduced into the host the therapeutic composition is at a temperature at which the viscosity of the therapeutic composition is smaller than 60 cP.

96. The method of Claim 94, wherein when the therapeutic composition is introduced into the host the therapeutic composition is at a temperature at which the viscosity of the therapeutic composition is smaller than 50 cP.

97. The method of Claim 94, wherein the therapeutic composition exhibits an increase in viscosity from smaller than 50 cP to larger than 70 cP with increasing temperature over the range of temperatures.

98. The method of Claim 83, wherein the therapeutic composition has reverse-thermal gelation properties and a reverse-thermal liquid-gel transition temperature in a range of from 1°C to the physiological temperature of the host.

99. The method of Claim 98, wherein when introduced into the host, the therapeutic composition is at a temperature below the reverse-thermal gel transition temperature where the viscosity of the therapeutic composition is no larger than 50 cP.

100. The method of Claim 83, wherein the therapeutic composition comprises a bioadhesive agent.

101. The method of Claim 83, wherein the therapeutic composition comprises a penetration enhancer.

102. The method of Claim 83, wherein the mucosal site is a rectal mucosal site and the introducing comprises introducing the therapeutic composition into the rectum of the host.

103. The method of Claim 85, wherein the therapeutic composition has reverse-thermal gelation properties, and when introduced into the rectum the therapeutic composition is at a temperature below a reverse-thermal gel transition temperature of the therapeutic composition.

104. The method of Claim 103, wherein the reverse-thermal gel transition temperature is no higher than the physiological temperature of the host.

105. The method of Claim 83, wherein the mucosal site is a vaginal mucosal site and the introducing comprises introducing the therapeutic composition into the vagina of the host.

5 106. The method of Claim 105, wherein the therapeutic composition has reverse-thermal gelation properties, and when introduced into the vagina the therapeutic composition is at a temperature below a reverse-thermal gel transition temperature of the therapeutic composition.

10 107. The method of Claim 106, wherein the reverse-thermal gel transition temperature is no higher than the physiological temperature of the host.

108. The method of Claim 83, wherein the mucosal site is a mucosal site within the bladder and the introducing comprises introducing the therapeutic composition into the bladder of the host.

15 109. The method of Claim 83, wherein the mucosal site is an ocular mucosal site and the introducing comprises applying at least one drop of the therapeutic composition to at an eye of the host.

110. The method of Claim 109, wherein the biocompatible polymer is a reverse-thermal gelation polymer not present in the therapeutic composition in sufficient quantity to impart reverse-thermal gelation properties to the therapeutic composition.

20 111. The method of Claim 83, wherein the mucosal site is within the oral cavity and the introducing comprises introducing the therapeutic composition into the oral cavity of the host.

25 112. The method of Claim 111 comprising, after the introducing, swishing the therapeutic composition in the mouth and thereafter ejecting from the mouth at least a portion of remaining of the therapeutic composition.

113. The method of Claim 111, wherein the mucosal site is sublingual and the introducing comprises sublingual placement of the therapeutic composition.

30 114. The method of Claim 111, wherein the therapeutic composition exhibits reverse-thermal viscosity behavior over at least some range of temperatures between 1°C and the physiological temperature of the host; and

when introduced into the oral cavity of the host, the therapeutic composition is at a temperature at which the viscosity of the therapeutic composition is smaller than 60 cP.

115. The method of Claim 83, wherein the mucosal site is an esophageal mucosal site and the introducing comprises introducing the therapeutic composition into the esophagus of the host.

116. The method of Claim 115, wherein the therapeutic composition has reverse-thermal gelation properties and a reverse-thermal gel transition temperature no higher than the physiological temperature of the host.

117. The method of Claim 115, wherein the introducing comprises introducing the therapeutic composition into the mouth of the host when the therapeutic composition is at a temperature where the therapeutic composition has a viscosity of at least 70 cP.

118. The method of Claim 115, wherein the therapeutic composition comprises a bioadhesive agent.

119. The method of Claim 118, wherein the bioadhesive agent is selected from the group consisting of poloxamers, mucin glycoproteins, trefoil peptides, cellulose derivatives and carbomers.

120. The method of Claim 118, wherein the bioadhesive agent comprises a carbophil polymer.

121. The method of Claim 83, wherein the mucosal site is a nasal mucosal site and the introducing comprises introducing the therapeutic composition into the nasal cavity of the host.

122. The method of Claim 121, wherein the introducing comprises introducing a spray of the therapeutic composition into the nasal cavity.

123. The method of Claim 121, wherein the therapeutic composition has reverse-thermal gelation properties and a reverse-thermal gel transition temperature that is no higher than the physiological temperature of the host; and

the method comprises forming the spray when the therapeutic composition is at a temperature that is lower than the reverse-thermal gel transition temperature.

124. The method of Claim 83, wherein the mucosal site is within the gastrointestinal tract and the introducing comprises introducing the therapeutic composition into the gastrointestinal tract of the host.

125. The method of Claim 83, wherein the mucosal site is a pulmonary mucosal site and the introducing comprises introducing the therapeutic composition into at least one lung of the host.

126. The method of Claim 125, wherein the introducing comprises inhaling the  
5 therapeutic composition in aerosol form.

127. The method of Claim 125, wherein the therapeutic composition has reverse-thermal gelation properties and a reverse-thermal gel transition temperature that is no higher than the physiological temperature of the host; and

the method comprises forming the aerosol form when the therapeutic composition is at a  
10 temperature that is lower than the reverse-thermal liquid-gel transition temperature.

128. The method of Claim 83, wherein the mucosal site is an aural mucosal site and the introducing comprises introducing the therapeutic composition into an ear of the host.

129. Use of the therapeutic composition of Claim 1 for prevention or treatment of mucositis.

130. Use of the therapeutic composition of Claim 1, for prevention or treatment of oral mucositis.

5        131. Use of the therapeutic composition of Claim 1, for prevention or treatment of esophagitis.

132. Use of the therapeutic composition of Claim 71 for prevention or treatment of mucositis.